REMARKS

An Office Action was mailed in the above-captioned application on April 24, 2006. Claims 1-5 and 7-12 are pending in the application. Claims 1-5 and 7-12 were rejected. This Amendment and Remarks document is submitted in response to said Office Action. Claims 1-3, 5, 7, and 8 have been amended, and claim 4 has been cancelled.

Drawings

The Examiner has objected to the drawings as failing to comply with the drawing requirement in that Figure 4A is not mentioned in the Brief Description of the Drawings. Page 21, lines 15-18, indicates that 4A shows electron microscopy of kidneys from an old transgenic mouse. The Brief description of the drawings has been amended to reflect this.

The Rejection under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-5 and 7-12 under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertain, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of § 112 requires that a patent application be written so as to "enable any person skilled in the art to which it pertains . . . to make and use the same." A specification is presumed to be enabling absent "a reason to doubt the objective truth of the statements contained therein." *In re Marzocchi*, 169 USPQ 367, 369 (C.C.P.A 1971). Further, a specification "may be enabling even though some experimentation is necessary," *United States v. Teletronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988), so long as the amount of experimentation required is not "undue experimentation." *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). The test is whether the specification "provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." *In re Wands*, 858 F. 2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Further, it is a tenet of patent law that an applicant need not teach what the skilled artisan already knows. Instead, it is preferred that an applicant "omit what is known in the art." *Hybritech Inc. v.*

Monoclonal Antibodies, 231 USPQ 81, 94 (Fed. Cir. 1986). With this standard in mind, the rejection raised by the Examiner are discussed below.

The rejection objects that since the claims are drawn to a non-human transgenic animal that is resistant to collagen induced arthritis prior to being modified to express the human FcγRIIA receptor, the animal must be at least a neonate and must therefore be genetically modified after birth. The rejection asserts that it was unknown in the art how to make a transgenic animal capable of germline transmission in a post partum animal.

The transgenic rodent is generated by traditional techniques of transgenesis rather than post-partum gene transfer. The amended claims clarify this point by reciting a "transgenic rodent generated by transgenically modifying an embryo from a strain that is resistant to collagen-induced arthritis, such that said rodent comprises and expresses a transgene for human FcγRIIa receptor, whereby the expression of said FcγRIIa renders the rodent susceptible to an autoimmune disease." Support for this amendment can be found, for example, at page 6, lines 24-25.

The rejection further asserts that only mice are used in the examples, while the claims encompass any non-human transgenic animal. The rejection reasons that there is not sufficient guidance to make other non-human transgenic animals and that the manufacture of transgenic animals with a given phenotype is sensitive to factors such as the integration site of the transgene, the copy number, and the genetic background of the animal. The rejection concludes that without guidance in how to make a transgenic animal with a specific phenotype, the claims are not enabled.

Claims 1-3 have been amended to remove the recitation of a non-human transgenic animal, and to recite instead, "a transgenic rodent." Support for this amendment can be found in the specification at page 6, lines 9-10. Claims 1-3 have also been amended to clarify the phenotype of the transgenic rodent. Namely, the claims have been amended to recite that the transgenic rodent comprises and expresses a transgene for human FcγRIIa receptor, whereby the expression of said FcγRIIa renders the rodent susceptible to an autoimmune disease.

The rejection indicates that even with respect to mice specifically, given the disclosure of the McKenzie, et al., (1999) *J. Immunol.* 162:4311-18 (which describes how to make transgenic mice with the FcγRIIA receptor), the possible variations in the phenotype of transgenic mice, and

the unpredictability in the field of mouse transgenics, that undue experimentation would be required to practice the claimed invention.

Regarding mice, McKenzie, et al., provides detailed procedures regarding the production of transgenic mice comprising and expressing the human FcγRIIa receptor. At least four transgenic mice expressing the human FcγRIIa receptor were generated, and one of these was chosen for further study (McKenzie, p. 4312, second column; page 4314, second column to page 4315). Given this disclosure, Applicant submits that one of ordinary skill in the art would be able to produce a transgenic mouse comprising and expressing the human FcγRIIa receptor without undue experimentation.

The rejection notes that in McKenzie, et al., the transgenic mouse line 32 had a 6-fold less induction of thrombocytopenia in response to antibody exposure than did mouse line 11. Applicant submits that this difference fails to support the rejection, since McKenzie, et al., reports that "[t]here was *no statisitically significant difference* in the nadir platelet counts induced by 4A5 between FcγRIIa transgenic line 11 and line 32." (p. 4316, col. 2, and legend to Fig. 6, emphasis added.).

Applicant further submits that is within the routine skill of the person having ordinary skill in the art to apply the present invention not only to mice, but to other rodent types such as rats and rabbits. No undue experimentation is required to produce non-mouse transgenic rodent equivalent to the transgenic mice exemplified in the present specification (i.e., non-mouse transgenic rodent expressing human FcγRIIa such that it is susceptible to an autoimmune disease), since techniques for transgenesis in non-mouse rodent species are well known and established, and further it is known that human FcγRIIa is bioactive in non-mouse rodents, as described in Bezdicek, et al., 1999 *Blood* 94:10 3448-55 (copy enclosed).

The rejection states that the specification does not state which mouse strains were used in the exemplary methods, and whether the mouse is an endogenous Fcγ knockout.

Applicant submits that that specification describes the transgenic mouse referred to in the Examples as one having a C57BL/6 and SJL genetic background. For example, the description of Figure 5 notes that the FcγRIIa transgenic mice have a G5FL/6 and SJL genetic background (page 8, lines 20-24). Also, page 6, lines 11-13 and page 17, lines 24-31 refer to a mouse derived from the strains C57BL/6 and SJL that has been modified to express the human FcγRIIa receptor. Page 17 also states that the mouse is characterized in McKenzie, et al. Page 18,

Example 1, paragraph (a) also references the genetic background of the mice and states that the transgenic mice are characterized in McKenzie, et al. Applicant submits that the mouse strains used are clearly defined in the specification. Furthermore, it clear from McKenzie, et al. that the transgenic mice were not engogenous Fcγ knockouts. In fact, McKenzie, et al., teaches that the transgenic mice were crossed with Fcγ knockout mice "to examine the role of FcγRIIa in immune clearance *in vivo* in the absence of FcγRI and FcγRIII." (page 4317, first column). The rejection asserts that the skilled practicioner would have to determine the effect of endogenous Fcγ receptors; however, the experiments of McKenzie, et al., clearly teach the effects of endogenous Fcγ receptors.

Regarding the rejection's assertion that it is not taught which of the mouse lines is resistant to collagen-induced arthritis prior to being genetically modified to express the human FcγRIIa receptor, applicant notes that Example 7 of the present specification teaches that mice having a C57BL/6 and SJL background are normally resistant to collagen-induced arthritis.

Applicant submits that it is well within the skill of the person having ordinary skill in the art to determine whether or a mouse strain with a given genetic background is susceptible to collagen-induced arthritis, then to transgenically modify those mice with FcγRIIa. Such animals could be routinely screened to identify those susceptible to an autoimmune disease. Reconsideration is respectfully requested.

The Rejection under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1, 2, and 7-9 under 35 U.S.C. § 102(b) as being anticipated by McKenzie, et al., 1999, *J. Immunol.* 162:4311-18. The Court of Appeals for the Federal Circuit has stated that anticipation requires the presence in a single prior art reference of each and every element of the claimed invention. *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1458 (Fed. Cir. 1984); *Alco Standard Corp. v. Tennessee Valley Auth.*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). "There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *Scripps Clinic v. Genentech Inc.*, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991) (citations omitted). As explained in detail below, Applicant believes that claim 1, as amended, is not anticipated by the prior art relied upon by the Examiner.

Claim 4 has been cancelled, and Claims 1 and 2 have been amended to recite the limitation of Claim 4, namely "wherein the compound reduces aberrant immune activity selected from the group consisting of aberrant immune complex formation, aberrant immune complex clearance and immune complex induced inflammation." Since Claim 4 was not rejected over McKenzie, et al., it is believed that the introduction of the limitation of Claim 4 into Claims 1 and 2 overcomes the rejection. Reconsideration is respectfully requested.

Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

Respectfully submitted,

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Enclosure

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